Visualization and identification of agonistic interaction through an exclusive transformation of sufficient component cause model

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Abstract

Sufficient-component cause (SCC) framework, as one of the most polished techniques for the methodology development of causal inference, has the advantage of visualizing the interaction effect by synergism or antagonism. However, it is well known that statistical interaction occurs even there is no synergism and antagonism, and vice versa. In this study, we propose a modified version of SCC, termed exclusive sufficient component causal (eSCC) model, and incorporate this model to counterfactual framework. The causal effects can be interpreted as the additive probabilities of conditions under eSCC. When two exposures of interest are considered, eSCC can visualize the existence of agonism, one important subtype of interaction other than synergism and antagonism. In addition, we further propose four approaches that suffice to identify and estimate the agonistic interaction: (1) To make a strong assumption that the synergism does not exist; (2) To exploit the information from a third factor by assuming that this factor is a necessary component for the background condition of synergistic interaction but is not involved in other mechanisms; (3) To consider a third factor necessary for the background condition of agonistic interaction but not involved in other mechanisms; and (4) To consider a risk factor that is assumed to be necessary for agonistic interaction of the two factors of interest but not involved in the mechanism of synergistic interaction or agonistically interacting with two factors. We applied the proposed methods to quantify the agonism of Hepatitis B and C virus (HBV and HCV) infections on liver cancer using a Taiwanese hepatitis cohort study (n = 23820). The result demonstrated that agonistic interaction is more dominant compared with synergistic interaction, which explains the findings that the dual infected patients do not have a significantly higher risk of liver cancer than those with single infection. This method fills the gap between causal interaction and mechanistic interaction and contributes to a comprehensive understanding of mechanistic investigation.